

Notice of Allowability

Application No.

09/175,683

Examiner

Richard Schnizer, Ph. D

Applicant(s)

CHEN ET AL.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 12/21/04.
2. ☒ The allowed claim(s) is/are 85-92.
3. ☒ The drawings filed on 20 October 1998 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date 12/21/04.
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in telephone interviews with Byron Olsen on 12/21/04 and 12/22/04

The application has been amended as follows:

IN THE CLAIMS:

Cancel claims 77-84.

Add the following:

Claim 85 (new): A method for producing *Plasmodium falciparum* protein MSP- 1 in milk of a non-human transgenic mammal, comprising:

1) providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said MSP-1 operably linked to a promoter which directs expression in a mammary gland and a signal sequence directing secretion of said MSP-1 into milk, wherein said modified nucleic acid sequence has been modified by replacing a number of AT-containing codons of a nucleic acid sequence encoding said MSP-1, as it naturally occurs in *Plasmodium falciparum*, with a codon or codons preferred by a mammalian cell for the purpose of expression and encoding the same amino acid as the replaced AT-containing codon or codons, wherein the number

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of codons replaced is sufficient to allow expression of said MSP-1 in said non-human transgenic mammal; and

2) allowing said non-human transgenic mammal to express said MSP-1 in its milk.

Claim 86 (new): A method for producing *Plasmodium falciparum* protein MSP- 1 in milk of a non-human transgenic mammal, comprising:

1) providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said MSP-1 operably linked to a promoter which directs expression in a mammary gland and a signal sequence directing secretion of said MSP-1 into milk, wherein said modified nucleic acid sequence has been modified by introduction of one or more silent mutations into a number of AUUUA mRNA instability motifs, as they naturally occur in *Plasmodium falciparum*, thereby eliminating said number of AUUUA instability motifs, allowing expression of said MSP-1 in said non-human transgenic mammal; and

2) allowing said non-human transgenic mammal to express said MSP-1 in its milk.

Claim 87 (new): A method for producing *Plasmodium falciparum* protein MSP- 1 in milk of a non-human transgenic mammal, comprising:

1) providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said MSP-1 operably linked to a promoter

which directs expression in a mammary gland and a signal sequence directing secretion of said MSP-1 into milk, wherein said modified nucleic acid sequence has been modified by:

a) replacing a number of AT-containing codons of a nucleic acid sequence encoding said MSP-1, as it naturally occurs in *Plasmodium falciparum*, with a codon or codons preferred by a mammalian cell for the purpose of expression and encoding the same amino acid as the replaced AT-containing codon or codons, and

b) introduction of one or more silent mutations into a number of AUUUA mRNA instability motifs, as they naturally occur in *Plasmodium falciparum*, thereby eliminating said AUUUA instability motifs,

wherein the number of said modifications is sufficient to allow expression of said MSP-1 in said non-human transgenic mammal; and

2) allowing said non-human transgenic mammal to express said MSP-1 in its milk.

Claim 88 (new): The method of claim 85, 86 or 87 wherein the modified nucleic acid further comprises at least one substitution of a glutamine codon for an asparagine codon, resulting in the loss of at least one N-glycosylation site in said MSP-1.

Claim 89 (new): A non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding *Plasmodium falciparum* protein MSP-1 operably linked to a promoter which directs expression in a mammary gland and a

signal sequence directing secretion of said MSP-1 into milk, wherein said modified nucleic acid sequence has been modified by replacing a number of AT-containing codons of a nucleic acid sequence encoding said MSP-1, as it naturally occurs in *Plasmodium falciparum*, with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as the replaced AT-containing codon or codons, wherein the number of codons replaced is sufficient to allow expression of said MSP-1 in said non-human transgenic mammal, and wherein said non-human transgenic mammal expresses said MSP-1 in its milk.

Claim 90 (new): A non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding *Plasmodium falciparum* protein MSP-1 operably linked to a promoter which directs expression in a mammary gland and a signal sequence directing secretion of said MSP-1 into milk, wherein said modified nucleic acid sequence has been modified by introduction of one or more silent mutations into a number of AUUUA mRNA instability motifs, as they naturally occur in *Plasmodium falciparum*, thereby eliminating said AUUUA instability motifs, allowing expression of said MSP-1 in said non-human transgenic mammal, and wherein said non-human transgenic mammal expresses said MSP-1 in its milk.

Claim 91 (new): The non-human transgenic mammal of claim 90 wherein said modified nucleic acid sequence is further modified by introduction of one or more silent mutations into a number of AUUUA mRNA instability motifs, as they naturally occur in

Plasmodium falciparum, thereby eliminating said AUUUA instability motifs, and allowing expression of said MSP-1.

Claim 92 (new): The non-human transgenic mammal of claim 89, 90, or 91 wherein the modified nucleic acid further comprises at least one substitution of a glutamine codon for an asparagine codon, resulting in the loss of at least one N-glycosylation site in said MSP-1.

Reference Cited

On 3/24/99 Applicant submitted a PTO 1449 listing Simons et al (Bio/Technology 6: 179-183, 1988). This document was not considered at the time of the first action. This reference has subsequently been considered and is made of record on the PTO 892 attached to this Action.

Specification

In the responses filed 2/19/03 and 7/24/03, Applicant requested deletion of the word "casine" at page 14, line 15 of the specification, and replacement with the correctly spelled word --casein--. This request was not carried out because "casine" does not occur at page 14, line 15 of the specification as filed, and the Examiner could not find it anywhere else either.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.



DAVE TRONG NGUYEN
PRIMARY EXAMINER